CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

20-364/SE8-016

Approval Letter

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug
Administration
Rockville MD 20857

NDA 20-364/S-016

Novartis Pharmaceuticals Corporation
Attention: Carl Schlotfeldt
One Health Plaza
East Hanover, NJ 07936-1080

Dear Mr. Schlotfeldt:

Please refer to your supplemental new drug application dated June 29, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lotrel (amlodipine and benazepril HCl) Capsules, 2.5/10mg, 5/10 mg, and 5/20 mg.

We acknowledge receipt of your submissions dated May 2 and 20, 2002. Your submission of May 20, 2002 constituted a complete response to our April 29, 2002 action letter.

This supplemental new drug application provides for a new, higher dosage strength that combines 10 mg of amlodipine with 20 mg of benazepril.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the submitted final printed labeling (package insert submitted May 20, 2002, and immediate container and carton labels submitted May 2, 2002). Accordingly, the supplemental application is approved effective on the date of this letter.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please call:

Ms. Denise M. Hinton
Regulatory Health Project Manager
(301) 594-5312.

Sincerely yours,

{See appended electronic signature page}

Douglas C.Throckmorton M.D.
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Doug Throckmorton
6/20/02 11:03:17 AM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER
20-364/SE8-016

Approvable Letter

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug
Administration
Rockville MD 20857

NDA 20-364/S-016

Novartis Pharmaceuticals Corporation
Attention: Mr. Carl Schlotfeldt
59 Route 10
East Hanover, New Jersey 07936-1080

Dear Mr. Schlotfeldt:

Please refer to your supplemental new drug application dated June 29, 2001, received July 2, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lotrel (amlodipine and benazepril HCl) Capsules.

We acknowledge receipt of your submissions dated July 17, October 26, and December 14, 2001 and February 20 and April 12, 15 and 17, 2002.

This supplemental new drug application proposes a new, higher dosage strength that combines 10 mg. of amlodipine with 20 mg. of benazepril.

We note your April 24, 2002 telephone conversation with Ms. Colleen LoCicero of this division in which you clarified that the proposed labeling in "pi.pdf" format in your April 17, 2002 submission is the correct version of the proposed labeling. The April 17, 2002 submitted proposed labeling in "pi.pdf" format was, therefore, the labeling reviewed for this supplemental application.

We have completed the review of this application, as amended, and it is approvable. Before this application may be approved, however, it will be necessary for you to submit final printed labeling (package insert and carton and container labels) revised as follows:

1. Please revise the storage statement on the carton and container labels for the new dosage strength to reflect the storage statement in your February 20, 2002 submitted revised draft package insert, as you committed to do in the correspondence that accompanied that submission.

2. Please replace the following paragraph that was added to the **ADVERSE REACTIONS** section of the package insert:

[redacted]

with the following:

> In a trial (n=386) comparing placebo, Lotrel 5/20, and Lotrel 10/20, edema and dizziness were most commonly reported in the Lotrel 10/20 group.

In addition, all previous revisions as reflected in the most recently approved labeling must be included. To facilitate review of your submission, please provide a highlighted or marked-up copy that shows the changes that are being made.

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL, ten of which individually mounted on heavy weight paper or similar material.

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

> Division of Drug Marketing, Advertising, and Communications, HFD-42
> Food and Drug Administration
> 5600 Fishers Lane
> Rockville, Maryland 20857

Within 10 days after the date of this letter, you are required to amend the supplemental application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

This product may be considered to be misbranded under the Federal Food, Drug, and Cosmetic Act if it is marketed with these changes prior to approval of this supplemental application.

If you have any questions, please call:

Colleen LoCicero
Regulatory Health Project Manager
(301) 594-5332.

Sincerely yours,

/S/

{See appended electronic signature page}

Douglas C. Throckmorton, M.D.
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Doug Throckmorton
4/29/02 12:48:16 PM